EXHIBIT L

Attorney Docket No.:16842-712

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application	PATENT APPLICATION
Inventor(s): Kenneth J. Livak et al.	
Application No.: 08/558,303	Group Art Unit: 1807
Filed: November 15, 1995	Examiner: D. Rees
Title: HYBRIDIZATION ASSAY USING SELF-QUENCHING FLUORESCENCE PROBE	

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Annette Granados (Signature)

Annette Granados

AMENDMENT UNDER 37 C.F.R. § 1.115

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Applicants submit this Amendment in response to the Examiner's Office Action mailed January 21, 1997 and Applicants' telephone interview with the Examiner on February 6, 1997. Also submitted herewith are new Figures 3, 4 and 5 and a Declaration under 37 C.F.R. § 1.132 by Kenji Asai. Reconsideration is respectfully requested in view of the following amendments and remarks.

IN THE FIGURES

Please add new Figures 3, 4 and 5.

IN THE SPECIFICATION

At page 1, line 18, after "November 16, 1994," insert --now U.S. Patent No. 5,538,848 --.

At page 11, after line 26, please insert

-- Figure 3 illustrates the functionalization of compound **5**.

Figure 4 illustrates the attachment of the spacer to polystyrene and CPG supports.

Figure 5 illustrates the labeling of the solid supports with TAMRA dye. --.

At pages 26-28, please delete Tables 2-4.

At page 29, line 5, please delete "Table 2" and insert --Figure 3--.

At page 29, line 7, please delete "Tables 3 and 4" and insert --Figures 4 and 5--.

At page 29, line 8, please delete "Table 2" and insert --Figure 3--.

At page 29, line 21, please delete "Tables 3 and 4" and insert --Figures 4 and 5--.

At page 35, line 16, please delete "Table 5" and insert --Table 2--.

At page 35, line 19, please delete "Table 5" and insert --Table 2--.

At page 37, line 6, please delete "Table 6" and insert --Table 3--.

At page 37, line 10, please delete "Table 6" and insert --Table 3--.

At page 38, line 1, please delete "Table 7" and insert --Table 4--.

At page 38, line 13, please delete "Table 7" and insert --Table 4--.

IN THE CLAIMS

Please delete claim 13.

Please amend the following claims.

1 1. (Thrice amended) A method for detecting a target polynucleotide in a sample comprising:

contacting [a] said sample of nucleic acids with an oligonucleotide probe under conditions [favorable for hybridization of] where said oligonucleotide probe

selectively hybridizes to said target polynucleotide, said oligonucleotide probe including [an oligonucleotide sequence capable of hybridizing to said target polynucleotide to be detected that does not hybridize with itself to form a hairpin structure under conditions used in a monitoring step of the method,] a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of said reporter molecule [, said oligonucleotide sequence existing in] which are attached to said oligonucleotide probe such that said oligonucleotide probe is capable of adopting at least one single-stranded conformation when [unhybridized] not hybridized to said target polynucleotide where said quencher molecule quenches the fluorescence of said reporter molecule [, said oligonucleotide sequence existing in] and is capable of adopting at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched[,] such that the fluorescence intensity of said reporter molecule when said oligonucleotide probe is hybridized to said target polynucleotide is greater than the fluorescence intensity of said reporter molecule when said oligonucleotide [sequence] probe is not hybridized to said target polynucleotide and said oligonucleotide probe is not hybridized with itself in the form of a hairpin structure; and

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monitoring the fluorescence of said reporter molecule [, an increase in the fluorescence intensity of said reporter molecule indicating the presence of said target polynucleotide] under conditions where said oligonucleotide probe does not hybridize with itself to form a hairpin structure in order to detect the hybridization of said target polynucleotide to said oligonucleotide probe.

22. (Amended) The method according to claim 1 wherein the fluorescence intensity of said reporter molecule under conditions where said oligonucleotide probe does not hybridize with itself to form a hairpin structure is at least about a factor of 6 greater when said oligonucleotide probe is hybridized to said target polynucleotide [is at least about a factor of 6 greater than the fluorescence intensity of said reporter molecule] than when said oligonucleotide probe is not hybridized to said target polynucleotide.

7 ~~7.~~ (Twice Amended) The method according to claim ~~1~~ 1 wherein said reporter molecule is attached to a 3' terminal nucleotide of said oligonucleotide [sequence] probe.

8 ~~8.~~ (Twice Amended) The method according to claim ~~7~~ 7 wherein said quencher molecule is attached to a 5' terminal nucleotide of said oligonucleotide [sequence] probe.

9 ~~9.~~ (Twice Amended) The method according to claim ~~1~~ 1 wherein said reporter molecule is attached to a 5' terminal nucleotide of said oligonucleotide [sequence] probe.

10 ~~10.~~ (Twice Amended) The method according to claim ~~9~~ 9 wherein said quencher molecule is attached to a 3' terminal nucleotide of said oligonucleotide [sequence] probe.

11 ~~11.~~ (Twice Amended) The method according to claim ~~1~~ 1 wherein said quencher molecule is attached to a 3' terminal nucleotide of said oligonucleotide [sequence] probe.

12 ~~12.~~ (Twice Amended) The method according to claim ~~1~~ 1 wherein said quencher molecule is attached to a 5' terminal nucleotide of said oligonucleotide [sequence] probe.

14 ~~15.~~ (Twice Amended) The method according to claim ~~1~~ 1 wherein said quencher is fluorescent and the fluorescence intensity of said reporter molecule is greater than the fluorescence intensity of said quencher molecule when said oligonucleotide [sequence] probe is hybridized to said target polynucleotide.

16 ~~17.~~ (Thrice amended) A method for detecting a target polynucleotide in a sample comprising:

contacting [a] said sample of nucleic acids with an oligonucleotide probe under conditions [favorable for hybridization of] where said oligonucleotide probe selectively hybridizes to said target polynucleotide, said oligonucleotide probe including [an oligonucleotide sequence capable of hybridizing to said target polynucleotide to be detected that does not hybridize with itself to form a hairpin structure under conditions used in a monitoring step of the method,] a fluorescent reporter molecule and a fluorescent quencher molecule capable of quenching the fluorescence of said reporter molecule [, said oligonucleotide sequence existing in] which are attached to said oligonucleotide probe such that said oligonucleotide probe is capable of adopting at least one single-stranded conformation when [unhybridized] not hybridized to said target polynucleotide where said fluorescent quencher molecule quenches the fluorescence of said reporter molecule [, said oligonucleotide sequence existing in] and is capable of adopting at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched[,] such that the ratio of the fluorescence intensities of said reporter molecule to said fluorescent quencher molecule when said oligonucleotide sequence is hybridized to said target polynucleotide is greater than the ratio of the fluorescence intensities of said reporter molecule to said fluorescent quencher molecule when said oligonucleotide [sequence] probe is not hybridized to said target polynucleotide and said oligonucleotide probe is not hybridized with itself in the form of a hairpin structure;

and

monitoring the ratio between the fluorescence of said reporter molecule and said fluorescent quencher molecule[, an increase in the ratio indicating the presence of the target polynucleotide] under conditions where said oligonucleotide probe does not hybridize with itself to form a hairpin structure in order to detect the hybridization of said target polynucleotide to said oligonucleotide probe.

~~17~~ 18. (Twice Amended) The method according to claim ~~17~~ 16 wherein the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said oligonucleotide [sequence] probe is hybridized to said target

polynucleotide is at least a factor of 6 greater than the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said oligonucleotide **[**sequence**]** probe is not hybridized to said target polynucleotide.

18 19. (Thrice amended) A method for detecting a target polynucleotide in a sample comprising:

contacting a sample of nucleic acids with an oligonucleotide probe attached to a solid support under conditions favorable for hybridization of said oligonucleotide probe to said target polynucleotide, said oligonucleotide probe including **[**an oligonucleotide sequence capable of hybridizing to said target polynucleotide to be detected that does not hybridize with itself to form a hairpin structure under conditions used in a monitoring step of the method,**]** a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of said reporter molecule **[**, said oligonucleotide sequence existing in**]** which are attached to said oligonucleotide probe such that said oligonucleotide probe is capable of adopting at least one single-stranded conformation when **[**unhybridized**]** not hybridized to said target polynucleotide where said quencher molecule quenches the fluorescence of said reporter molecule **[**, said oligonucleotide sequence existing in**]** and is capable of adopting at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched**[**,**]** such that the fluorescence intensity of said reporter molecule when said oligonucleotide probe is hybridized to said target polynucleotide is greater than the fluorescence intensity of said reporter molecule when said oligonucleotide **[**sequence**]** probe is not hybridized to said target polynucleotide and said oligonucleotide probe is not hybridized with itself in the form of a hairpin structure; and

monitoring the fluorescence of said reporter molecule **[**, an increase in the fluorescence intensity of said reporter molecule indicating the presence of said target polynucleotide**]** under conditions where said oligonucleotide probe does not hybridize with itself to form a hairpin structure in order to detect the hybridization of said target polynucleotide to said oligonucleotide probe.

20. (Amended) The method according to claim 19 wherein the fluorescence intensity of said reporter molecule under conditions where said oligonucleotide probe does not hybridize with itself to form a hairpin structure is at least about a factor of 6 greater when said oligonucleotide probe is hybridized to said target polynucleotide [is at least about a factor of 6 greater than the fluorescence intensity of said reporter molecule] than when said oligonucleotide probe is not hybridized to said target polynucleotide.

24 ~~25~~. (Twice Amended) The method according to claim ~~19~~ 18 wherein said reporter molecule is attached to a 3' terminal nucleotide of said oligonucleotide [sequence] probe.

25 ~~26~~. (Twice Amended) The method according to claim ~~25~~ 24 wherein said quencher molecule is attached to a 5' terminal nucleotide of said oligonucleotide [sequence] probe.

26 ~~27~~. (Twice Amended) The method according to claim ~~19~~ 18 wherein said reporter molecule is attached to a 5' terminal nucleotide of said oligonucleotide [sequence] probe.

27 ~~28~~. (Twice Amended) The method according to claim ~~27~~ 26 wherein said quencher molecule is attached to a 3' terminal nucleotide of said oligonucleotide [sequence] probe.

~~28~~ 29. (Twice Amended) The method according to claim ~~19~~ 18 wherein said quencher molecule is attached to a 3' terminal nucleotide of said oligonucleotide [sequence] probe.

~~29~~ ~~30~~. (Twice Amended) The method according to claim ~~19~~ 18 wherein said quencher molecule is attached to a 5' terminal nucleotide of said oligonucleotide [sequence] probe.

36 ~~37.~~ (Twice Amended) The method according to claim 18 wherein said quencher molecule is fluorescent and the fluorescence intensity of said reporter molecule is greater than the fluorescence intensity of said quencher molecule when said oligonucleotide [sequence] probe is hybridized to said target polynucleotide.

38 ~~39.~~ (Thrice amended) A method for detecting a target polynucleotide in a sample comprising:

contacting [a] said sample of nucleic acids with an oligonucleotide probe attached to a solid support under conditions [favorable for hybridization of] where said oligonucleotide probe selectively hybridizes to said target polynucleotide, said oligonucleotide probe including [an oligonucleotide sequence capable of hybridizing to said target polynucleotide to be detected that does not hybridize with itself to form a hairpin structure under conditions used in a monitoring step of the method,] a fluorescent reporter molecule and a fluorescent quencher molecule capable of quenching the fluorescence of said reporter molecule [, said oligonucleotide sequence existing in] which are attached to said oligonucleotide probe such that said oligonucleotide probe is capable of adopting at least one single-stranded conformation when [unhybridized] not hybridized to said target polynucleotide where said fluorescent quencher molecule quenches the fluorescence of said reporter molecule [, said oligonucleotide sequence existing in] and is capable of adopting at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched[,] such that the ratio of the fluorescence intensities of said reporter molecule to said fluorescent quencher molecule when said oligonucleotide sequence is hybridized to said target polynucleotide is greater than the ratio of the fluorescence intensities of said reporter molecule to said fluorescent quencher molecule when said oligonucleotide [sequence] probe is not hybridized to said target polynucleotide and said oligonucleotide probe is not hybridized with itself in the form of a hairpin structure; and

monitoring the ratio between the fluorescence of said reporter molecule and said fluorescent quencher molecule[, an increase in the ratio indicating the

presence of the target polynucleotide] under conditions where said oligonucleotide probe does not hybridize with itself to form a hairpin structure in order to detect the hybridization of said target polynucleotide to said oligonucleotide probe.

REMARKS

The present Amendment is in response to the Examiner's Office Action mailed January 21, 1997. Claim 13 is canceled and claims 1, 2, 7-12, 15, 17-20, 25-30, 37 and 39 are amended. Claims 1-12 and 14-40 are pending in view of the above amendments.

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

I. Examiner Interview on February 6, 1997

Applicants wish to express their appreciation to the Examiner for conducting a telephone interview with the undersigned attorney on February 6, 1997.

II. Priority

As requested by the Examiner, Applicants amend the first paragraph of the Specification to update the status of the parent application.

III. Information Disclosure Statement

Applicants traverse the Examiner's refusal to consider JP 5123195 on the grounds that a concise statement of relevance was provided in the form of the abstract to this reference which was submitted with the IDS. Also provided herewith is a Declaration under 37 C.F.R. §1.132 which provides a concise statement of the relevance of JP 5123195. Applicants respectfully request the Examiner to indicate JP 5123195 as having been considered in view of the abstract and the Rule 132 Declaration.

IV. Objection To The Specification

The Examiner objects to the Specification on the grounds that it contains matter in tables which should be presented in the figures. In response, Applicants amend the Specification and submit new Figures 3, 4 and 5 in order to move Tables 2-4 into the figures. Withdrawal of the Examiner's objection in view of the amendments to the Specification and the submission of Figures 3, 4 and 5 is respectfully requested.

V. Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 1-40 under 35 U.S.C. § 112, Second Paragraph as being indefinite.

With regard to the independent claims (claims 1, 17, 19, 39), the Examiner states that the phrase "conditions favorable for hybridization" renders the claims indefinite with regard to the metes and bounds of the hybridization conditions. These claims have been amended to specify that the sample of nucleic acids is contacted with an oligonucleotide probe under conditions where the oligonucleotide probe selectively hybridizes to the target polynucleotide. Applicants submit that these claims are not indefinite in view of this amendment to the claims and respectfully request that this ground of rejection be withdrawn.

The Examiner also states that the phrase "hybridize with itself" renders the claims indefinite because the claims are unclear with regard to whether the entire probe sequence or only a subunit of the sequence hybridizes with itself. In order to clarify this point, Applicants amend the independent claims to remove reference to an oligonucleotide sequence. Instead, the claims state that the oligonucleotide probe hybridizes to the target polynucleotide and does not hybridize with itself to form a hairpin structure

The Examiner also objects to Applicants' use of the term "includes" with regard to the reporter and quencher molecules. In response, Applicants amend the independent claims to specify that the reporter and quencher molecules are attached to the oligonucleotide probe.

The Examiner also indicates that a word appears to be missing between the words "unquenched" and "the fluorescent intensity." In response, Applicants insert

the words "such that" in order to clarify the relationship between the phrases preceding and following the inserted phrase.

With regard to claim 13, the Examiner objects to a lack of antecedent basis in the claim with regard to the nucleic acid polymerase. In response, Applicants delete claim 13.

With regard to claim 17, the Examiner objects that the quencher is not specified as being fluorescent. In response, Applicants amend claim 17 to specify a fluorescent quencher.

VI. Rejection Under 35 U.S.C. § 102(b) (Heller,et al.)

The Examiner rejects claims 1, 2, 15 and 16 under 35 U.S.C. § 102(b) as being anticipated by Heller, et al.

Claim 1 specifies a method for detecting a target polynucleotide which **monitors the fluorescence of a reporter molecule** (donor) where the fluorescence intensity of the reporter molecule (donor) is designed to **increase** when the probe is hybridized to the target polynucleotide.

By contrast, Heller, et al. **monitors the fluorescence of the quencher molecule** (acceptor) and teaches designing probes where the quencher (acceptor) efficiently quenches the fluorescence of the reporter molecule (donor) when hybridized to a target polynucleotide so that the quencher (acceptor) is strongly fluorescent when hybridized to a target. For example, Figures 1 and 3 of Heller, et al. illustrate a probe where the donor and acceptor molecules are in close proximity so that energy is efficiently transferred to the acceptor. Figures 2, 4 and 5 of Heller, et al. illustrate dual probes where the donor and acceptor molecules come into close proximity when hybridized to the target. Heller, et al. thus teaches away from the method of the present invention by focusing on probes which provide efficient fluorescence transfer between the reporter (donor) and quencher (acceptor) molecules. Applicants therefore submit that claims 1, 2, 15 and 16 are not anticipated by Heller, et al.

VII. Rejection Under 35 U.S.C. § 102(b) (Bagwell,et al.)

The Examiner rejects claims 1-16 under 35 U.S.C. § 102(b) as being anticipated by Bagwell, et al.

Bagwell, et al. teaches a probe which is designed to form a hairpin structure when the probe is not hybridized to a target polynucleotide so that the reporter and quencher molecules are kept close to each other in order to insure that energy transfer occurs.

Independent claim 1 claims a method where the fluorescence of the reporter molecule is monitored **under conditions where the oligonucleotide probe does not hybridize with itself to form a hairpin structure**. Since Bagwell, et al. does not teach a probe where the reporter and quencher molecules come close enough to each other **without** forming a hairpin structure for energy transfer to occur, as specified in claim 1, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Bagwell's use of a hairpin structure also teaches away from the present invention by effectively teaching to one of ordinary skill that a hairpin structure is required in order for energy transfer to occur. Since Bagwell, et al. teaches in the direct opposite direction as the present invention, Applicants submit that the present invention is not rendered obvious by Bagwell, et al.

VIII. Rejection Under 35 U.S.C. § 102(b) (HITACHI LTD)

The Examiner rejects claims 1 and 15 under 35 U.S.C. § 102(b) as being anticipated by HITACHI LTD (JP 5123195). As indicated in the telephone interview with the Examiner on February 6, 1997, the Examiner's rejection is based upon the English language abstract to HITACHI LTD which specifies a method for detecting DNA or RNA which uses a probe labeled with an energy donor and energy receptor. In the method, a "change of fluorescence in the energy donor or the energy receptor by the energy transfer by the presence of hybrid formation which the labeled DNA or RNA is detected."

Applicants traverse the Examiner's rejection on the grounds that the English language abstract to HITACHI LTD does not teach each and every limitation as specified in claims 1 and 15 so as to render these claims anticipated. Specifically,

the abstract does not specify that the fluorescence of the reporter molecule increases when the probe is hybridized to the target **and** that the fluorescence of the reporter molecule is monitored under conditions where the oligonucleotide probe does not hybridize with itself to form a hairpin structure. On this basis, the Examiner has not set forth a *prima facie* case for anticipation.

In order to clarify the actual teaching of the HITACHI LTD reference, Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 by Kenji Asai in which a concise statement of the relevance of HITACHI LTD (JP 5123195) is provided. As specified in the Rule 132 Declaration,

> HITACHI LTD does not teach an oligonucleotide probe which includes a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of the reporter molecule where the fluorescent reporter molecule and quencher molecule are attached to the oligonucleotide probe such that the oligonucleotide probe is capable of adopting at least one single-stranded conformation when not hybridized to the target polynucleotide where the quencher molecule quenches the fluorescence of the reporter molecule and is capable of adopting at least one conformation when hybridized to the target polynucleotide where the fluorescence of the reporter molecule is unquenched such that the fluorescence intensity of the reporter molecule when the oligonucleotide probe is hybridized to the target polynucleotide is **greater** than the fluorescence intensity of the reporter molecule when the oligonucleotide probe is not hybridized to the target polynucleotide **and** the oligonucleotide probe is not hybridized with itself to form a hairpin structure.
>
> HITACHI LTD also does not teach monitoring the fluorescence of the reporter molecule under conditions where the oligonucleotide probe does not hybridize with itself to form a hairpin structure and the fluorescence intensity of the reporter molecule is **greater** when the oligonucleotide probe is hybridized to the target polynucleotide.
>
> Rather, in one embodiment, HITACHI LTD teaches a probe, as illustrated in Figure 2, where the fluorescence intensity of the reporter molecule when the oligonucleotide probe is hybridized to the target polynucleotide is **less** than the fluorescence intensity of the reporter molecule when the oligonucleotide probe is not hybridized to the target polynucleotide. In this embodiment, a **decrease** in the fluorescence intensity of the reporter molecule is used to indicate the presence of the target polynucleotide.

HITACHI LTD also teaches a probe, as illustrated in Figure 3, which hybridizes with itself to form a hairpin structure when not hybridized to the target polynucleotide.

Since HITACHI LTD does not teach a probe which has a reporter molecule with increased fluorescence intensity when the probe is not hybridized to the target **and** does not hybridize with itself to form a hairpin structure under the monitoring conditions, as specified in amended claim 1, Applicants submit that HITACHI LTD does not anticipate claims 1 or 15. In view of these distinctions, Applicants respectfully request that the Examiner withdraw the present rejection under 35 U.S.C. § 102(b).

IX. Rejection Under 35 U.S.C. § 103 Of Claims 14, 17-18

The Examiner rejects claims 14 and 17-18 under 35 U.S.C. § 103 as being unpatentable over Heller, et al. or Bagwell, et al. As discussed above in Sections VI and VII, both Heller, et al. and Bagwell, et al. teach away from the present invention. Unlike the present invention, Heller, et al. monitors the quencher (acceptor) as opposed to the reporter molecule and designs probes whose reporter molecule (donor) are less fluorescent when hybridized to a target. Meanwhile, Bagwell, et al. teaches probes which are designed to form hairpin structures when not hybridized to the target. Since both Heller, et al. and Bagwell, et al. teach away from independent claim 1, Applicants submit that dependent claims 14 and 17-18 are not rendered obvious by Heller, et al. or Bagwell, et al.

X. Rejection Under 35 U.S.C. § 103 Of Claims 19-20 and 32-39

The Examiner rejects claims 19-20 and 32-39 under 35 U.S.C. § 103 as being unpatentable over Heller, et al. in view of Sheridan, et al. As discussed above in Sections VI and IX, Heller, et al. teaches away from the probes used in the present invention. Meanwhile, Sheridan is relied upon by the Examiner for teaching the immobilization of the probes on a solid support. Since Heller, et al. teaches away from the probes used in the method and Sheridan, et al. does not teach modifying the Heller probes to arrive at the probes of the present invention,

Applicants submit that claims 19-20 and 32-39 are not rendered obvious by the combination of Heller, et al. and Sheridan, et al.

XI. Rejection Under 35 U.S.C. § 103 Of Claims 19-40

The Examiner rejects claims 19-40 under 35 U.S.C. § 103 as being unpatentable over Bagwell, et al. in view of Sheridan, et al. As discussed above in Sections VII and IX, Bagwell, et al. teaches away from the probes used in the present invention by designing them to form hairpins at the monitoring temperature of the method. Meanwhile, Sheridan is relied upon by the Examiner for teaching the immobilization of the probes on a solid support. Since Bagwell, et al. teaches away from the probes used in the method and Sheridan, et al. does not teach modifying the Bagwell probes to arrive at the probes of the present invention, Applicants submit that claims 19-20 and 32-39 are not rendered obvious by the combination of Heller, et al. and Sheridan, et al.

CONCLUSION

In light of the Amendments and the arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: March 14, 1997

David J. Weitz
Reg. No. 38,362

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1505
(415) 493-9300